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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/578,744

06/20/2006

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EXAMINER

PIHONAK, SARAH

ART UNIT

PAPER NUMBER

1627

NOTIFICATION DATE

DELIVERY MODE

02/01/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/578,744	Applicant(s) YOKOZAWA ET AL.	
	Examiner SARAH PIHONAK	Art Unit 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 December 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-17 and 19-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-17 and 19-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/11/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a national stage entry of PCT/JP04/17998, filed on 11/26/2004.

Priority

This application claims foreign priority to 2003-398201, filed on 11/27/2003.

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/11/2009 has been entered.

Response to Remarks

2. Applicant's arguments filed 12/11/2009 have been fully considered but they are not persuasive. The Applicants have argued that the instant claims would not have been prima facie obvious to one of ordinary skill in the art, at the time of the invention, over Andersson et. al., in view of Nohira et. al., because Andersson et. al. discloses working examples of the hydrogenation of an ester of α -alkoxycinnamic acid with Pd/C, and not with the chiral metal complexes claimed. However, a reference is not considered only for the working examples disclosed, but also for the teachings and disclosure as a whole. Andersson et. al. teaches that the asymmetric hydrogenation of α -alkoxy carboxylic ester compounds can be successfully performed with chiral catalysts such as Rh-BINAP, or [Et-DuPHOS-Rh(COD)]. Nohira et. al. teaches that chiral rhodium and

ruthenium complexes are both used for the asymmetric hydrogenation of α,β -unsaturated carboxylic acids. As such, it would have been prima facie obvious for one of ordinary skill in the art, to employ chiral ruthenium complexes for the asymmetric hydrogenation of α -alkoxy cinnamic acids, because Nohira et. al. teaches that both ruthenium and rhodium chiral complexes are used for catalytic asymmetric hydrogenations; therefore, one would have expected success in substituting the chiral rhodium complexes taught by Andersson et. al. for chiral ruthenium complexes for the asymmetric hydrogenation of the α -alkoxy cinnamic acids. The Applicants have also asserted that the claimed metal complexes successfully catalyze the asymmetric hydrogenation to prepare phenylpropionic acids with % ee values of 90% and 88.6%, respectively; however, it is noted that the claims do not recite % ee values. Future claim amendments reciting % ee values of the reaction which are supported by the disclosure will be considered by the examiner.

3. The Applicants have argued that contrary to the teachings of Andersson et. al., the stereoselective asymmetric hydrogenation of α -alkoxy cinnamic acids is difficult and challenging, as indicated by the references disclosed on the Information Disclosure Statement submitted on 12/11/2009. These references have been considered; it is also acknowledged that the reference of Chen et. al., (Angewandte Chem., 46, p. 4143, Table 2, 2007), teaches the asymmetric hydrogenation of α -alkoxy cinnamic acids with chiral rhodium complexes, with high % ee values. Therefore, these references do not discredit the teachings of Andersson et. al. The rejection of the claims under 35 USC § 103(a) as being unpatentable over Andersson et. al., in view of Nohira et. al., was

proper. It is noted that the claims have been amended to recite specific chiral ruthenium complexes for the asymmetric hydrogenation process. In consideration of these claim amendments, a modified rejection under 35 USC § 103(a) has been made, which will be discussed in detail further in this action. This action is made NON-FINAL.

Claims 1-9 and 18 have been cancelled by the Applicants; claims 10-17 and 19-22 are pending.

4. Claims 10-17 and 19-22 were examined.

5. Claims 10-17 and 19-22 are rejected.

Claim Rejections-35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

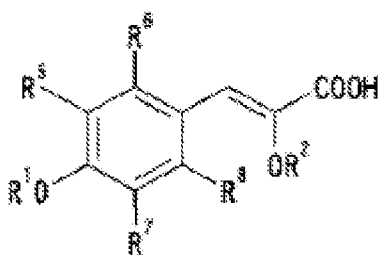
8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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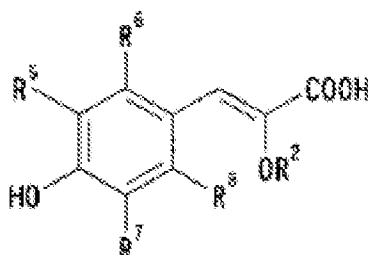
the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 10-17 and 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andersson et. al., US Patent No. 6,258,850, in view of Saburi et. al., US Patent No. 5,334,758.

10. The instant claims are directed to a process for producing optically active phenyl propionic acids through asymmetric hydrogenation of the compounds of formula (4) and formula (9) as shown below:



(4)

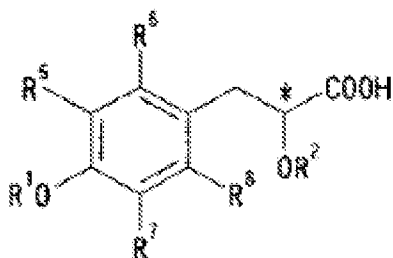


(9)

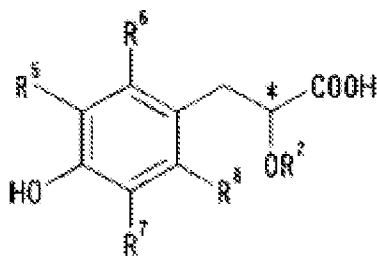
Where R^1 =protecting group; R^2 =alkyl group; R^5 - R^8 =H. The instant claims are also drawn to carrying out the hydrogenation in the presence of a chiral ruthenium complex, such as $Ru_2Cl_4[(S)\text{-}H_8\text{-binap}]_2NEt_3$ or $Ru_2Cl_4[(R)\text{-}H_8\text{-binap}]_2NEt_3$, and that the resulting hydrogenated products, which are shown as compounds of formula (5) and (6) below,

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are further recrystallized after synthesis with solvents selected from hydrocarbons, alcohols, ketones, water, or mixtures thereof.

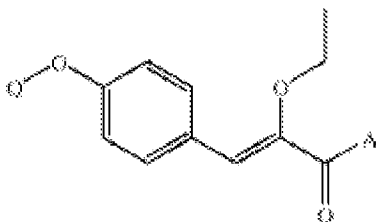


(5)

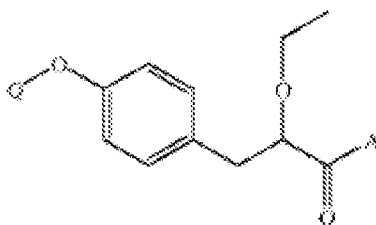


(6)

Andersson et. al. teaches that compounds of formula (VII) below can successfully undergo asymmetric hydrogenation to form compounds of formula (V), which is also shown below:



(VII)



(V)

Where A=OH; Q=H or a protecting group (column 4, lines 29-46; column 7, line 50-column 8, line 24). The compounds taught by Andersson et. al. includes the compounds instantly claimed. Andersson et. al. teaches that the asymmetric hydrogenation reaction is conducted in the presence of chiral transition metal catalysts such as Rh-BINAP, [Et-DuPHOS-Rh(COD)], as well as a variety of other catalysts (column 8, lines 17-24).

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Crystallization of the products with solvents such as ethanol, isopropanol, and hydrocarbons and mixtures of solvents is taught (column 4, lines 66-67; column 13, lines 34-37; column 14, lines 42-45; column 15, lines 41-44). Andersson et. al. also teaches that the asymmetric hydrogenation can be performed in a wide variety of solvents (column 8, lines 25-32), and that protecting groups can be removed (column 5, lines 35-57).

While Andersson et. al. teaches that asymmetric hydrogenation can be successfully performed on compounds such as those instantly claimed, with chiral rhodium complexes and other metal catalysts, chiral ruthenium complexes such as $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ are not explicitly taught.

Saburi et. al. teaches a process for preparing optically active carboxylic acids, through the asymmetric hydrogenation of α , β -unsaturated carboxylic acids with a chiral metal phosphine complex (Abstract). The metals used for the complex include ruthenium, rhodium, and palladium, with preference given to the ruthenium complexes of the formula shown below (column 2, line 64-column 3, line 6):



Where $\text{R}^4=\text{H}$, and Y =tertiary amine, such as triethylamine (column 3, lines 6-32). Saburi et. al. explicitly teaches that $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ are used to prepare optically active carboxylic acids (column 3, lines 41-43, and 56 and 58).

One of ordinary skill in the art, at the time of the invention, would have been motivated to use the complexes $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ taught by Saburi et. al., for the asymmetric hydrogenation of the compounds of formula

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(VII) taught by Andersson et. al., because Andersson et. al. teaches that such compounds can undergo asymmetric hydrogenation with chiral rhodium complexes, and Saburi et. al. teaches that $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ are used to catalyze the hydrogenation of α , β -unsaturated carboxylic acids with high stereoselectivity. As the compounds taught by Andersson et. al. are α , β -unsaturated carboxylic acids, one of ordinary skill in the art would have expected success in using complexes such as $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ to catalyze the asymmetric hydrogenation. Saburi et. al. also teaches that chiral rhodium complexes can be successfully used for the hydrogenation, but that preference is given to the ruthenium phosphine complexes. As such, it would have been prima facie obvious to replace the chiral rhodium complexes taught by Andersson et. al. with the chiral ruthenium complexes $\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ or $\text{Ru}_2\text{Cl}_4[(\text{R})\text{-H}_8\text{-binap}]_2\text{NEt}_3$ for the asymmetric hydrogenation of compounds of formula (VII), with the expectation of improved optical purity.

Information Disclosure Statement

11. The information disclosure statement (IDS) submitted on 12/11/2009 was filed after the mailing date of the final rejection on 9/11/2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-every other Friday 8:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/

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Supervisory Patent Examiner, Art Unit 1627